

# Safety and efficacy of mesenchymal stem cell (MSC) therapy in symptom management of multiple sclerosis as compared to the currently approved medications



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## Abstract

In MS, a chronic demyelinating autoimmune disease, myelin is destroyed and is unable to be repaired. Current treatments focus on symptom alleviation and can cause many undesirable side effects. Mesenchymal stem cells (MSCs) are currently being investigated for their remyelination properties in MS. The studies selected for this research all aimed to assess safety as their primary objective. Though some minor adverse events were experienced, the MSC treatment did not lead to any major life-threatening events. The majority of the studies demonstrated significantly improved lesion volume on MRI and EDSS scores. Participants reported feeling better than they had prior to the study. Some studies have suggested using MSCs in conjunction with the currently approved medication as an option for treatment. It's important to continue to study this topic and pursue the best possible treatment and care options for those suffering from MS.

## Introduction

Neurons in the body are responsible for generating and conducting the electrical impulses which control our body's functions and information processing. Neuronal axons are surrounded by a myelin sheath, which is vital for proper conduction of the impulses throughout the body. In MS, a chronic demyelinating autoimmune disease, the myelin is destroyed and is unable to be repaired. Current treatments for MS only focus on symptom alleviation and can cause many undesirable side effects. Mesenchymal stem cells (MSCs) are becoming more widely used in various treatments today thanks to their many unique properties. Recently, researchers have been directing their attention toward the use of MSCs in remyelination therapy for chronic MS patients.

## Methods

Several searches on PubMed and Ovid were conducted to find articles relevant to the topic. The initial search included human clinical trials from the last five years and each article was then evaluated and excluded via the following criteria

- Studies including systematic reviews or meta-analysis.
- Any articles featuring other inflammatory or autoimmune diseases besides MS.
- Any studies involving treatment forms other than MSCs. 7 studies met this exclusion criteria and were utilized in the study.

## Results

1. Llifriu, S, et al.
  1. Randomized double blind control trial with 9 subjects
2. Dahbour, S, et al.
  1. Open label prospective trial with 15 subjects
3. Harris, VK, et al.
  1. Open label single arm clinical trial with 20 subjects
4. Riordan, NH, et. Al.
  1. Open label single arm clinical trial with 20 subjects
5. Cohen, JA, et al.
  1. Open label pre/post comparison study with 24 subjects
6. Jin-Feng Li, et al.
  1. Randomized two arm control trial with 23 subjects
7. Fernández, O, et al.
  1. Placebo controlled triple blind study with 34 subjects

All of the selected studies shared a primary objective of assessing safety, many also assessing the efficacy of treatment as a secondary objective. All trials were successfully completed. Though some minor adverse events were experienced, the MSC treatment did not lead to any major life threatening events. The majority of the studies demonstrated significantly improved lesion volume on MRI, as well as significantly improved EDSS scores.

### C. Comparison of results

Study	EDSS Score	MRI Lesion Volume	T25-FW	9HP
Llifriu, S, et al.	NS	S	N/A	N/A
Dahbour, S, et al.	NS	S	NS	S
Harris, VK, et al.	NS	S	S	S
Riordan, NH, et. al.	S	NS	S	S
Cohen, JA, et al.	NS	S	N/A	N/A
Jin-Feng Li, et al.	S	N/A	N/A	N/A
Fernández, O, et al.	NS	NS	N/A	N/A

### Key

EDSS-Expanded Disability Status Scale; T25-FW-Timed 25-Foot Walk; 9HP-9 Hole Peg; S-significant; NS-not significant

## Discussion

While the studies failed to show significant outcomes and improvements in all the analyzed data, some significant results were seen and prove very promising. Many participants reported feeling better than they had prior to the study while being treated with MSCs. Some studies have suggested using MSCs in conjunction with the currently approved medication as an option for treatment. Until these questions can be fully addressed, it's important to continue to study this topic and pursue the best possible treatment and care options for those suffering from MS.

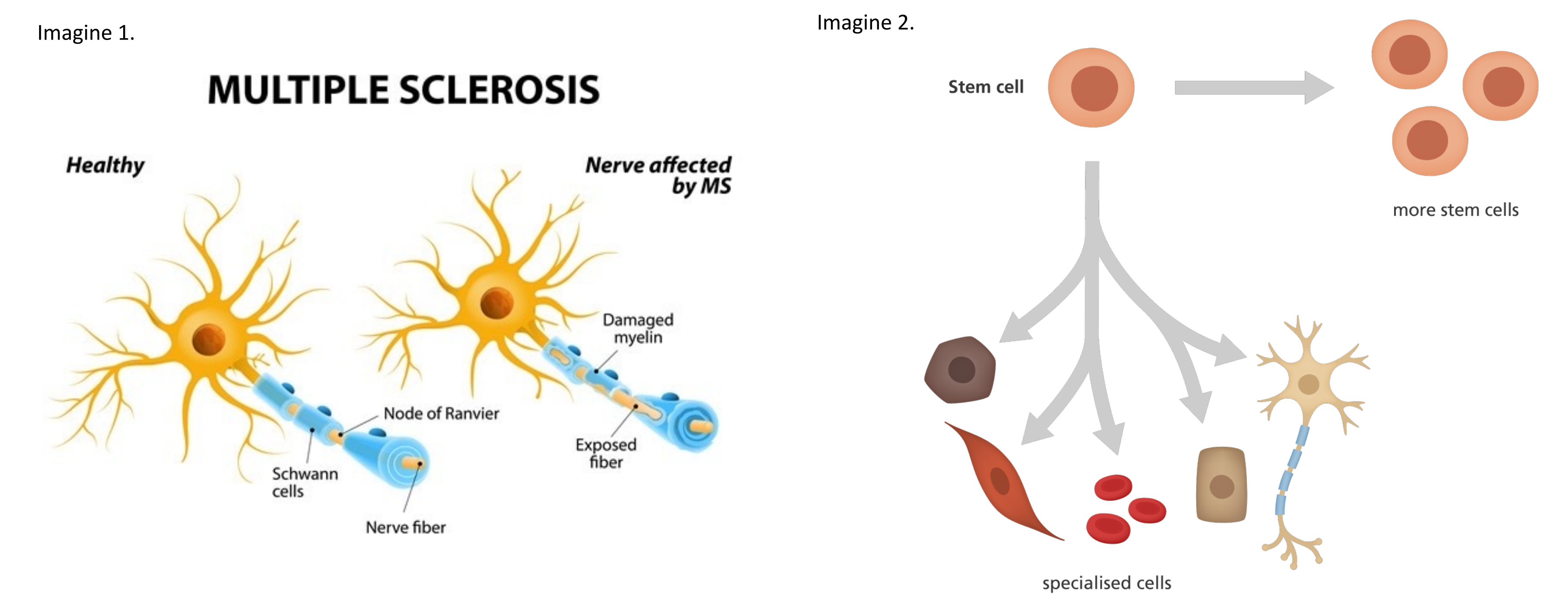


Image 1: Types of Multiple Sclerosis (MS). News-Medical  
Imagine 2: What is a Stem Cell?. Your Genome

## Conclusion

The primary objective of the majority of the chosen studies was to assess the safety of MSC in the treatment of MS. Very few adverse effects were demonstrated in any of the studies, all of which resolved without need for intervention or treatment cessation. This is a promising aspect of the research, as it allows this research to move forward confidently. The most important next step in this field is to continue to expand the number of participants to gain more significant results. While the studies failed to show significant outcomes and improvements in all the analyzed data, some significant results were seen and prove very promising. Many participants reported feeling better than they had prior to the study while being treated with MSCs. It remains to be seen if this is the effect of bias, but further studies which blind participants can perhaps eliminate that possibility. If results were to remain significant, it would be a great leap forward in this area of study.

- References:
1. Love, S. Demyelinating disease. *Journal of Clinical Pathology*.
  2. Montalban, X. M.D., et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. *New England Journal of Medicine*.
  3. Balasa, R. et al. An Intricate Mechanism of Action of Avonex in Relapsing Remitting Multiple Sclerosis Patients: Variation of Serum Titre of Interleukin-17A, Interleukin-10 and Transforming Growth Factor- $\beta$ . *CNS Neurological Disorders Drug Targets*.
  4. Walther, E.U. Hohlfeld, R. Multiple sclerosis: side effects of interferon beta therapy and their management. *Neurology*.
  5. Stahlke, A. M., et al. Ocrelizumab: A New B-cell Therapy for Relapsing Remitting and Primary Progressive Multiple Sclerosis. *Annals of Pharmacotherapy*.
  6. J. Liu, et al. Fibrin scaffolds containing ectomesenchymal stem cells enhance behavioral and histological improvement in a rat model of spinal cord injury. *Cells Tis. Organs*.
  7. Zhang, Zhijian, et al. Nasal ectomesenchymal stem cells: multi-lineage differentiation and transformation effects on fibrin gels. *Biomaterials*.
  8. Llifriu, S, et al. Randomized placebo-controlled phase I trial of autologous mesenchymal stem cells in multiple sclerosis. *PLOS ONE*.
  9. Dahbour, S, et al. Mesenchymal stem cells and conditioned media in the treatment of multiple sclerosis patients: Clinical, ophthalmological and radiological assessments of safety and efficacy. *CNS Neuroscience and Therapeutics*.
  10. Harris, VK, et al. Phase I Trial of Intrathecal Mesenchymal Stem Cell-derived Neural Progenitors in Progressive Multiple Sclerosis. *The Lancet: EBioMedicine*.
  11. Riordan, NH, et al. Clinical feasibility of umbilical cord tissue-derived mesenchymal stem cells in the treatment of multiple sclerosis. *Journal Of Translation Medicine*.
  12. Cohen, JA, et al. Pilot trial of intravenous autologous culture-expanded mesenchymal stem cell transplantation in multiple sclerosis. *Multiple Sclerosis Journal*.
  13. Jin-Feng Li, et al. The Potential of Human Umbilical Cord-Derived Mesenchymal Stem Cells as a Novel Cellular Therapy for Multiple Sclerosis. *Cell Transplantation*.
  14. Fernández, O, et al. Adipose-derived mesenchymal stem cells (AdMSC) for the treatment of secondary-progressive multiple sclerosis: A triple blinded, placebo controlled, randomized phase I/II safety and feasibility study. *PlosOne*.
  15. Chervvethy, Susha. Types of Multiple Sclerosis (MS). News-Medical.
  16. What is a stem cell? Your Genome.